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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/891,602	06/26/2001	Alexey B. Dyatkin	ORT-1451	2105

27777 7590 03/16/2004

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EXAMINER	
AULAKH, CHARANJIT	
ART UNIT	**PAPER NUMBER**
1625	22

DATE MAILED: 03/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/891,602	Applicant(s) DYATKIN ET AL.	
	Examiner Charanjit S. Aulakh	Art Unit 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19,21-36,44-46 and 48-58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19,21-23,25,26,32-36,44-46 and 48-58* is/are rejected.

7)☒ Claim(s) *24 and 27-31* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. According to paper no. 20 filed on Feb. 9, 2004, the applicants have filed a RCE.

2. Claims 1-19, 21-36, 44-46 and 48-58 are now pending in the application.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-19, 21-23, 25, 26, 32-36, 44-46 and 48-58 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating asthma, rheumatoid arthritis, inflammatory bowel disease and atherosclerosis using instant compounds where variables together (R2 and R3 or R3 and R4 or R3 and R5 or R4 and R5 or A and R3 or A and R4 or A and R5) do not form a monocyclic ring, does not reasonably provide enablement for treating all known inflammatory, autoimmune and cell-proliferative diseases and furthermore, for treating asthma, rheumatoid arthritis, inflammatory bowel disease and atherosclerosis using instant compounds where variables together (R2 and R3 or R3 and R4 or R3 and R5 or R4 and R5 or A and R3 or A and R4 or A and R5) do form a monocyclic ring. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The following eight different factors (see Ex parte Foreman, 230 USPQ at 547; Wands, In re, 858.F.2d 731, 8 USPQ 2d 1400, Fed. Cir. 1988) must be considered in order for the specification to be enabling for what is being claimed:

Quantity of experimentation necessary, the amount of direction or guidance provided, presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability and the breadth of claims. In the instant case, the specification is not enabling based on atleast four of the above mentioned eight factors such as quantity of experimentation necessary, the amount of direction or guidance provided, presence or absence of working examples, the state of the prior art and the breadth of claims.

The instant compounds are antagonists of alpha4beta1 and alpha4beta7 receptors as demonstrated in the specification and therefore, will have utility in treating disease conditions where hyperactivity of these receptors is well known in the prior art or alternatively where these antagonists have been demonstrated to be efficacious in animal models of specific disease conditions such as asthma, rheumatoid arthritis, inflammatory bowel disease or atherosclerosis. There is no teaching either in the specification or prior art that hyperactivity of these receptors occurs in all known inflammatory, autoimmune or cell-proliferative disorders. There is no teaching either in the specification or prior art that compounds having antagonist activity at alpha4beta1 and alpha4beta7 receptors show efficacy in animal models of all known inflammatory, autoimmune or cell-proliferative disorders. There is no teaching in the specification that what specific diseases are mediated by hyperactivity or hypersecretion of integrins. There are no working examples to show how the instant compounds having antagonist activity at alpha4beta1 and alpha4beta7 receptors in vitro will have utility in treating all known inflammatory, autoimmune or cell-proliferative disorders when administered in

vivo since in vivo activity depends upon several factors such as absorption, metabolism etc.The instant compounds of formula (I) encompass hundreds of thousands of compounds based on variables R1-R6, B1, B2 and Y and therefore, in absence of such teachings in the specification or prior art, it would require undue experimentation to demonstrate the effectiveness of the instant compounds in treating all known inflammatory, autoimmune ,cell-proliferative and integrin -mediated disorders.

In regard to lack of enablement for treating asthma, rheumatoid arthritis, inflammatory bowel disease and atherosclerosis using instant compounds where variables together (R2 and R3 or R3 and R4 or R3 and R5 or R4 and R5 or A and R3 or A and R4 or A and R5) do form a monocyclic ring, there is not even a single compound prepared or exemplified out of 96 exemplified compounds in the specification where these variables do form a ring. Furthermore, the experimental in vitro data is also obtained using instant compounds where these variables do not form a monocyclic ring and shows large variation in Ki values for tested compounds. As mentioned above, instant compounds encompass hundreds of thousands of compounds based on these variables where these variables even do not form a monocyclic ring. Therefore, the instant compounds of formula (I) will encompass additional hundreds of thousands of compounds when variables R1-R5 and A do form monocyclic rings containing 1-3 heteroatoms. In absence of teachings or working examples in the specification, it would require undue experimentation to demonstrate the effectiveness of the instant compounds of formula (I) where these variables do form a monocyclic ring for antagonist activity at alpha4beta1 and alpha4beta7 receptors and hence their utility.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-19, 21-23, 25, 26, 32-36, 44-46 and 48-58 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In independent claims 1, 24 and 25, the values of variables R2-R5, R7, R9, R10 and R14 defined as ----heteroaryl or heterocyclyl----is indefinite since the size of the ring, number and types of heteroatoms present in the ring are not defined.

In independent claims 1, 24 and 25, the term ---comprise--- used for variables R2-R5 is inclusive or open-ended and does not exclude additional unrecited elements or method steps; see Moleculon Research Corp. v. CBS, Inc.,793 F.2d 1261, 229 USPQ 805 (Fed. Circ. 1986), MPEP 211.03.

In claims 1, 7-9, 24 and 25, the term ---optionally present---- used for variable R6 is vague. The applicants are suggested to include ---hydrogen--- as one of the substituents for this variable R6.

In claims 46, 48-56 and 58, the term ---integrin mediated disoder--- is indefinite since the disorders are not defined. The specification does not teach any disorder which is mediated by integrin.

Allowable Subject Matter

7. Claims 24 and 27-31 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charanjit S. Aulakh whose telephone number is (571)272-0678. The examiner can normally be reached on Monday through Friday, 8:30 A.M. to 5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571)272-0699. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

C. S. Aulakh

Charanjit S. Aulakh
Primary Examiner
Art Unit 1625